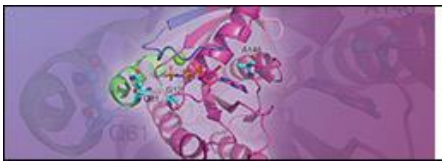

Current as of March 17, 2023

Short Talks Selected from Proffered Abstracts

PR01 **Structural plasticity of KRAS oncogenic mutants – a case of misleading conclusions from GTP analogues.** Alok K. Sharma. NCI RAS Initiative, Frederick National Laboratory for Cancer Research, Frederick, MD, United States.

PR02, A035 **Factors modulating RAF dimerization downstream of RAS – A mechanistic overview.** Jawahar Sudhamsu. Genentech Inc., South San Francisco, CA, United States.

PR03, B010 **Cooperative anti-tumor effects of combined inhibition of KRAS^{G12C} plus autophagy in preclinical models of KRAS^{G12C}-driven lung cancer.** Phaedra C. Ghazi. University of Utah, Salt Lake City, UT, United States.

PR04, A024 **A bimodal mechanism of RAS inactivation by monoubiquitination.** Wout Magits. VIB-KULeuven Center for Cancer Biology, Leuven, Belgium.

PR05 **The role of the RAS GTPase RIT1 in RASopathies and cancer.** Pau Castel. New York University School of Medicine, New York, NY, United States.

PR06, A034 **Germline RASopathy mutations provide insights into the differential regulation of RAF family kinases.** Russell Spencer-Smith. National Cancer Institute-Frederick, Frederick, MD, United States.

PR07 **Oncogenic Kras signaling shapes the tumor microenvironment in lung adenocarcinoma.** Rachael K. Baliira. University of Michigan, Ann Arbor, MI, United States.

PR08 **TCR1020 specific for KRAS G12V restricted to HLA-A*11:01 exhibits potent and precise antigen specificity for clinical development.** Adham S. Bear. University of Pennsylvania, Philadelphia, PA, United States.

PR09 **KRAS-targeted PROTAC degraders are broadly efficacious against KRAS-dependent tumor models.** Kathryn Smith. Arvinas Operations, Inc., New Haven, CT, United States.

PR10, B041 **IK-595, a MEK-RAF complex inhibitor, obviates CRAF mediated resistance resulting in superior RAS/MAPK pathway inhibition and anti-tumor activity in RAS/RAF altered cancers.** X. Michelle Zhang. Ikena Oncology, Boston, MA, United States.

Poster Session A
(To be presented on March 6 from 4:45-7:00 p.m. ET)

[R] – Remote Presentation

A001 **RAS:RAF proximity ligation assay may predict response to KRAS^{G12C} inhibitors in NSCLC.** Ryoji Kato. H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, United States.

A002 **Early changes in circulating cell free *KRAS* G12C as a possible blood-based response biomarker for Adagrasib in non-small cell lung cancer (NSCLC).** Yanan Kuang. Dana Farber Cancer Institute, Boston, MA, United States.

A003 **COVALENT-102: A phase 1/1b dose finding study of BMF-219, an oral covalent menin inhibitor, in patients with metastatic non-small cell lung cancer (NSCLC), pancreatic cancer (PDAC), & colorectal cancer (CRC) with activating KRAS mutations.** Stacey A. Cohen. Fred Hutchinson Cancer Center, Seattle, WA, United States.

A004 ***KRAS* allelic imbalance drives an epithelial MAPK-dependent tumor initiation program that is inefficient in provoking metastasis in colorectal cancer *in vivo*.** Arafath K. Najumudeen. Cancer Research UK Beatson Institute, Glasgow, Scotland.

A005 **Canine hemangiosarcoma as a model for RAS-mutated human cancers: Preliminary data.** Garrett Harvey. The One Health Company, Palo Alto, CA, United States.

A006 **Chromatin remodeling as a potential epigenetic mechanism of tolerance to KRAS loss.** Flavia Martins. FMUP/i3S/IPATIMUP/Northwestern University, Porto, Portugal.

A007 **Proteogenomic landscape of KRAS^{G12C} lung adenocarcinomas reveals new subtypes and potential combination therapies.** Paul A. Stewart. Moffitt Cancer Center, Tampa, FL, United States.

A009 **AFNT-111: a novel TCR-engineered T cell therapy targeting the oncogenic driver KRAS G12V.** Michele Hoffmann. Affini-T Therapeutics, Watertown, MA, United States.

A010 **Using oncogenic pathway agonism to sensitize *RAS*-mutant cancers to immunotherapy. [R]** Kenneth Y. Tsai. H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, United States.

A012 **Exploring the role of adaptive amino acid responses in Ras-driven leukemia progression and therapy.** Ji Zhang. Wells Center for Pediatric Research, Indianapolis, IN, United States.

A013 **Role of EGFR in KRAS-mediated resistances in colorectal cancer.** Emi Adachi-Fernandez. Center for Cancer Research, Medical University of Vienna, Vienna, Austria.

A014 **Inhibition of Kras^{G12D} with a novel small molecule inhibitor alters the pancreatic cancer microenvironment.** Samantha B. Kemp. University of Pennsylvania, Philadelphia, PA, United States.

A015 **Dynamics and lipid interactions of the RAS-RBD-CRD protein complex.** Felice C. Lightstone. Lawrence Livermore National Lab, Livermore, CA, United States.

A016 **Expanded RAS proteoform landscape in malignant cell lines revealed by top-down mass spectrometry.** Caroline J. DeHart. Frederick National Laboratory for Cancer Research, Frederick, MD, United States.

A017 **Deciphering the role of integrated stress response (ISR) in the developmental stages of mutant KRAS lung cancer.** Jia Yi Zou. Lady Davis Institute at the Jewish General Hospital, Montréal, QC, Canada.

A018 **A top-down proteomic assay to evaluate KRAS4B-compound engagement.** Robert A. D'Ippolito. Frederick National Laboratory for Cancer Research, Frederick, MD, United States.

A019 **The role of KRAS ubiquitination in lung cancer heterogeneity.** Tonci Ivanisevic. KU Leuven - VIB CCB, Leuven, Belgium.

A020 **CETSA profiling unveils novel targets engaged by anti-tumor drug rigosertib to inhibit RAS-MAPK signaling and trigger NLRP3 inflammasome activation.** Petros Kechagioglou. Cell Biology Unit, University Medical Center Mainz, Mainz, Germany.

A022 **Translation initiation factor 2B (eIF2B) stimulates mutant KRAS function in cancer.** Hyungdong Kim. 1.Lady Davis Institute for Medical Research, Sir Mortimer B. Davis-Jewish General Hospital, Montreal, QC, Canada. 2.Division of Experimental Medicine, Department of Medicine, Faculty of Medicine, McGill University, Montréal, QC, Canada.

A023 **Structural basis for regulation of MAPK signaling by DUSP5 and DUSP6.** Jennifer E. Kung. Genentech, South San Francisco, CA, United States.

A024 **A bimodal mechanism of RAS inactivation by monoubiquitination.** Wout Magits. VIB-KULeuven Center for Cancer Biology, Leuven, Belgium.

A025 **Investigating the molecular mechanisms of regulation of the RAS guanine nucleotide exchange factor, SOS1 by Grb2 and 14-3-3.** Orlando E. Martinez. Genentech, Inc., San Francisco, CA, United States.

A026 **Stochastic phenotypes in RAS-dependent developmental diseases.** Robert A. Marmion, Princeton University, Princeton, NJ.

A027 **Defining the role of PER1 and circadian rhythm dysregulation in KRAS/LKB1-mutant lung adenocarcinoma.** Rebecca E. Parker. Emory University, Atlanta, GA, United States.

A028 **An isogenic H/N/KRAS-less mouse embryonic fibroblast cell line panel derived from a size sorted diploid clonal parent.** Katie Powell. Frederick National Laboratory for Cancer Research, Frederick, MD, United States.

A029 **Unfolding the role of cell state on stress granule heterogeneity and function in KRAS-driven pancreatic cancer.** Alexandra Redding. Thomas Jefferson University, Philadelphia, PA, United States.

A031 **KRAS (G12C) mediated mRNA translation program.** Kamini Singh. Albert Einstein College of Medicine, Bronx, NY, United States.

A032 **Targeting RAS beyond KRAS, a review. [R]** Neetu Singh. King George Medical University, Lucknow, India.

A033 **KRAS codon 12 oncogenic mutations modulate protein conformation within the Switch II/Helix3 pocket.** Brian Smith. Frederick National Laboratory for Cancer Research, Frederick, MD, United States.

A034 **Germline RASopathy mutations provide insights into the differential regulation of RAF family kinases.** Russell Spencer-Smith. National Cancer Institute-Frederick, Frederick, MD, United States.

A035 **Factors modulating RAF dimerization downstream of RAS – A mechanistic overview.** Jawahar Sudhamsu. Genentech Inc., South San Francisco, CA, United States.

A036 **Oncogenic mutations in BRAF and MEK weaken the ATP-stabilized inactive conformation of RAF to promote RAF dimerization and MAPK pathway activation.** Timothy J. Wendorff. Genentech, South San Francisco, CA, United States.

A037 **Oncogenic RAS signals from lysosomes to activate mTORC1 in multiple myeloma.** Ryan M. Young. National Cancer Institute, Bethesda, MD, United States.

A039 **RAS signaling strength determines phenotypic response in the colon.** Amanda R. Moore. Genentech, South San Francisco, CA, United States.

A040 **The SRG OncoRat supports growth of numerous RAS mutant cell lines, expanding pre-clinical RAS-inhibitor testing.** R. Grace Walton, Hera BioLabs, Lexington, KY.

Poster Session B
(To be presented on March 7 from 4:45-7:00 p.m. ET)

B002 **Development of bifunctional CRBN-SOS1 degraders for treatment of mutant KRAS cancers.** Kyle Begovich. Biotheryx, San Diego, CA, United States.

B003 **Combined inhibition of the MAPK and Hippo pathways drives efficacious tumor suppression in a faithful model of mutant *Kras* (KPC) PDAC.** Deepavali Chakravarti. StellanovaTherapeutics Inc., Houston, TX, United States.

B004 **Multi-omics profiling to identify mechanisms of resistance to KRAS inhibition: A comparative study on colorectal and lung cancer.** Saikat Chowdhury. The University of Texas MD Anderson Cancer Center, Houston, TX, United States.

B005 **RAS inhibitors to treat Luminal B breast cancer.** Tariq Arshad, Qualigen Therapeutics, Carlsbad, CA, United States.

B006 **Novel direct RAS inhibitors for pancreatic cancer.** Tariq Arshad, Qualigen Therapeutics, Carlsbad, CA, United States.

B007 **Proximal RTK signaling regulates tumor initiating cell survival and therapeutic responsiveness in EGFR- and KRAS-mutated lung adenocarcinoma.** Brianna Daley. USUHS, Bethesda, MD, United States.

B009 **TEAD inhibition overcomes YAP1/TAZ-driven resistance to RAS inhibitors in $KRAS^{G12C}$-mutant cancers.** Alexander C. Edwards. University of North Carolina at Chapel Hill, Chapel Hill, NC, United States.

B010 **Cooperative anti-tumor effects of combined inhibition of $KRAS^{G12C}$ plus autophagy in preclinical models of $KRAS^{G12C}$-driven lung cancer.** Phaedra C. Ghazi. University of Utah, Salt Lake City, UT, United States.

B012 **Effects of adagrasib on oncogenic signaling, immune cell regulation and biomarkers of response in preliminary clinical analyses.** Jill Hallin. Mirati Therapeutics, San Diego, CA, United States.

B013 **Exploring the switch II pocket of KRAS(G12D) with mutant-selective monobody inhibitors.** Takamitsu Hattori. NYU Langone Health, New York, NY, United States.

B014 **Phenotypic CRISPR genome-wide screening for the discovery of genetic regulators of allele-specific mutant KRAS.** Xiyue Hu. Northwestern, Chicago, IL, United States.

B015 **Wildtype RAS activity and PI3K signaling as new vulnerabilities in cells with acquired resistance to Sotorasib.** Denis Imbody. H. Lee Moffitt Cancer Center, Tampa, FL, United States.

B016 **High throughput application of the NanoBiT Biochemical Assay for the discovery of selective p110α isoform binders that block its interaction with KRAS.** Mohamed (Soly) S. Ismail. Francis Crick Institute / AstraZeneca, London / Cambridge, United Kingdom.

B018 **The Development of macrocyclic peptide Ras inhibitors.** Kristopher Josephson. Unnatural Products, Inc, Santa Cruz, CA, United States.

B019 **ASO-mediated NRAS knockdown overcomes gilteritinib late resistance in *FLT3*-AML.** Sunil K. Joshi. Oregon Health & Science University, Portland, OR, United States.

B020 **Creating actionable neoantigens by design with KRAS(G12C) covalent inhibitors.** Shohei Koide. New York University Langone Health, New York, NY, United States.

B021 **Pan-RAS IMM-1-104 activity in humanized 3D tumor models is independent of specific amino acid substitution.** Brett Hall. Immuneering Corporation, San Diego, CA, United States.

B022 **A non-conserved histidine residue on KRAS drives paralog selectivity of the KRAS G12D inhibitor MRTX1133.** Ji Luo. National Cancer Institute, Bethesda, MD, United States.

B023 **Inhibition of RAS signaling and tumorigenesis through targeting novel vulnerabilities.** John P. O'Bryan. Medical University of South Carolina, Charleston, SC, United States.

B024 **Combined inhibition of farnesyltransferase and MEK is effective in fusion-negative HRAS-mutant rhabdomyosarcoma.** Patience Odeniyide. The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University School of Medicine, Baltimore, MD, United States.

B025 **The RAF/MEK clamp avutometinib (VS-6766) enhances antitumor efficacy of KRAS G12C and G12D inhibitors through vertical inhibition of RAS, RAF and MEK.** Jonathan A. Pachter. Verastem Oncology, Needham, MA, United States.

B026 **Overcoming KRAS G12C inhibitor resistance with chaperone-mediated protein degrader in NSCLC.** Ines Pulido. University of Illinois Chicago, Chicago, IL, United States.

B027 **Bioluminescence resonance energy transfer (BRET) as a tool for assessing mutant KRAS-effector affinity and drug efficacy.** Megan E. C. Rigby. Frederick National Laboratory for Cancer Research, Frederick, MD, United States.

B028 **Pharmacological inhibition of USP9X as a novel targeted therapy for *RIT1*-driven lung adenocarcinoma and other cancers.** Amanda Riley. Fred Hutch Cancer Center, Seattle, WA, United States.

B029 **Functional analysis of the role of RAP1GDS1 and RhoA in KRAS-driven lung adenocarcinoma.** Marta Roman Moreno. University of California San Francisco, San Francisco, CA, United States.

B030 **Using the ResCu system for preclinical testing of KRAS G12C inhibitors.** Victor M. Ruiz. resistanceBio, San Carlos, CA, United States.

B031 **Inhibition of mutant RAS via Myotubularin Related Protein 7-mimicking peptide.** Daniel Saar. REPIN and Structural Biology and NMR Laboratory (SBiNLab), Linderstrøm-Lang Centre for Protein Science, Department of Biology, University of Copenhagen, Copenhagen, Denmark.

B032 **KRAS copy number variation and mutant allele fractions predict *in vitro* response of PDX-derived human pancreatic cancer cell lines to KRAS^{G12D} inhibitor MRTX1133.** Bhaswati Sarcar. H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, United States.

B033 **Wild-type RAS signaling is an essential therapeutic target in *RAS*-mutated cancers.** Nancy Sealover. USUHS, Bethesda, MD, United States.

B034 **Determination of KRAS- and ERK-regulated phosphoproteomes in KRAS-mutant cancers.** Clint A. Stalnecker. University of North Carolina at Chapel Hill, Chapel Hill, NC, United States.

B035 **Targeting transcriptional elongation kinases prevents adaptation to KRAS^{G12C} inhibitors in both MAPK-dependent and -independent models of acquired resistance.** Yaakov E. Stern. H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, United States.

B036 **Treatment modalities in KRAS-driven cancer.** Darren R. Tyson. Vanderbilt School of Medicine, Nashville, TN, United States.

B037 **Hit-finding by Cysteine-Scanning (HCS): a method for finding druggable pockets.** Laurens Moore van Tienen. Broad Institute of MIT and Harvard/Dana-Farber Cancer Institute/Harvard Medical School, Boston, MA, United States.

B038 **Preclinical efficacy of KRASG12C inhibitors in models of pediatric cancer.** Marielle Yohe. NCI, Frederick, MD, United States.

B039 **BIO-PROTAC: Application of cell penetrating scFv to treat undruggable KRAS mutant cancer.** Gookjin Yoon. Seoul National University, Seul, Republic of Korea.

B040 **Designed sensors reveal normal and oncogenic Ras signaling in endomembranes and condensates.** Jason Z. Zhang. University of Washington, Seattle, WA, United States.

B041 **IK-595, a MEK-RAF complex inhibitor, obviates CRAF mediated resistance resulting in superior RAS/MAPK pathway inhibition and anti-tumor activity in RAS/RAF altered cancers.** X. Michelle Zhang. Ikena Oncology, Boston, MA, United States.